GMO Task Force
Report To Health Commission

08 May 2006

Table of Contents

Introduction

During the Measure Q campaign in 2004 much information and disinformation was presented to the public via various forums. The Health Commission was one of those forums. After the measure was defeated, the Health Commission felt it would be useful to have a task force gather scientifically based information regarding the health implications of GMO foods and crops. The GMO Task Force was formed as a working group to gather the aforementioned data and compile it into a report.

Mission Statement

To provide the people of San Luis Obispo County with scientifically based information regarding the health implications of genetically engineered foods and crops.

Goals

1. To gather reviewed scientific information on genetically engineered foods and crops. (eg. health effects, epidemiological studies, product labeling and marketing).
2. To conduct liaison with Health Officer, Ag Commissioner, Supervisor Bianchi and other appropriate agencies and entities regarding genetically engineered foods and crops.
1. To work with the Education Committee (Health Commission) to provide educational opportunities to the public on this topic.
2. To update the Health Commission on the current status of the Task Force findings at 4 months, 8 months and 12 months (as appropriate). A "Final Report" will be presented for consideration to the full Health Commission, setting forth scientific information (Pro and Con) on the subject of genetically engineered foods/crops from the perspective of the health considerations and implications.
3. To take no position (Pro or Con) as to whether the County should have legislation on genetically engineered foods and crops.

Given the above goals, the task force set the following objectives:

1. Sufficiently educate task force members in the scientific, regulatory and political issues surrounding GMO crop technology
2. Collection of scientifically-based research and conclusions (pro and con) on the health effects of GMO crops.
3. Learning and documenting concerns from the public through open monthly meetings and requests for supporting information.
4. Providing balanced reports to the Health Commission based in evidence, rather than prediction.
5. With the Education Committee of the Health Commission provide public educational opportunities.

The task force met eleven times from May of 2005 thru April 2006. The original members were as follows:

- •Lynn Enns, RN – Chair
- •Michael Broadhurst, Ph.D
- •Penny Chamousis, Health Commissioner Alternate
- •John Doyle
- •Jeffrey Hiner, DC
- •Sara Horne, Health Commissioner
- •Marc Lea, Liaison to the SLO Agriculture Commission
- •Robert Robbins, M.D., D.D.S., FAAOHNS
- •Scott Steinmaus, Ph.D.

Added in January of 2006 were:

- Gere diZerega, MD
- Ralph Jacobson, PhD
- Michelle Shoresman, Liason to the Public Health Department

In order to meet their objectives, the task force set out to identify relevant scientific issues and public concerns through invited speakers and public comment periods; and to analyze and discuss relevant literature.

Through comments and presentations at meetings as well as correspondence from concerned individuals, several recurring themes of concern presented themselves:

1. Uncertainty that government regulations, laws and standards are adequate to protect the public.
2. Expressed opinion that labeling is needed.
3. Concern about standardization of testing protocols and compliance review.
4. Risk assessment versus the precautionary principal.
5. General distrust of transgenic science.
6. Fear of unintended effects, particularly allergic reactions.
7. Fear of contamination of food crops by crops not intended for human consumption.
8. Concern about antibiotic resistance markers.
9. Suspicion that genetically engineered crops have increased-not decreased- the use of chemicals in agriculture.
10. Concern regarding the possibility of increased susceptibility of children to unknown adverse effects.

Many of the above listed concerns are addressed in several areas of this report. The sections of the report have been written by different individuals with input and review by the task force as a whole. Each section or group of sections has an appropriate bibliography.

Government regulations, laws and standards

The mission statements and goal of the Health Commission of San Luis Obispo County were quite specific. In the preparation of this portion of the report every attempt was made to answer the questions posed by the FDA approval process. Frequently the documents associated with this task were either used verbatim or paraphrased as accurately as possible. Many sources were used as reference beyond the included bibliography here, but present in the GMO Task Force Archives. Opinions presented in Task Force meetings where used as points of concern to be answered in this portion of the report. Every attempt was made to utilize this input accurately and reflect it within this report. This portion of the report IN NO WAY represents a position taken by the author or any other member of the Task Force. Its goal is to provide timely information and direction to further resources for communities of the County of San Luis Obispo.

In 1992 the FDA published its first extensive policy guideline, "Statement of Policy: Foods Derived from New Plant Varieties". In this first major report on foods derived from bioengineering the FDA attempts to describe the application of current existing laws (FD&C) regarding food safety to bioengineered (GM) foods.

"Bioengineered foods and food ingredients must adhere to the same standards of safety under the FD&C (Federal Food, Drug and Cosmetic Act) that apply to their conventionally bred counterparts. This means that these products must be as safe as the traditional foods on the market. FDA has broad authority to initiate regulatory action if a product fails to meet the requirements of the FD&C act."

<u>FDA relies on two sections of the FD&C act to govern both traditional and bioengineered food;</u>

"The adulteration provisions of section 402 (a) (1). Under this <u>post market</u> authority FDA has the power to remove a food from the market (or sanction those marketing the food) if the food poses a risk to public health. It is important to note that the FD&C Act places a legal duty on developers to ensure that the foods they market to consumers are safe and comply with all legal requirements."

The second is "The food additive provisions in section 409. Under this section, a substance that is intentionally added to food is a food additive, unless the substance is generally recognized as safe (GRAS) or is otherwise exempt (e.g., a pesticide, the safety of which is overseen by the EPA). Unapproved food additives are subject to the adulteration provisions in 402 (a) (2) of the FD&C Act".

<u>The FD&C Act requires that there is pre-market approval of any additive, regardless of the technique used to add it to food.</u>

Using the above as the general basis for FDA consideration of food products to be brought to the market place, "There are no FDA pre-market approval requirements for foods generally", no matter what techniques are used to develop them.

<u>THE PROCESS</u>
This section should be reviewed with the preliminary statements above fully reviewed and understood regarding applicable FD&C laws and new food products. A more complete explanation of the "VOLUNTARY CONSULTATIVE" process is found in bibliography articles #2, 4, 5, 9, 13.
The "voluntary consultative process" appears to be misunderstood and frequently misinterpreted. The process is initiated by the manufacturer of a new product <u>voluntarily</u> prior to the entering of the

marketplace of the new food product. In the initial 1992 FDA Statement of Policy there is no pre-entry time limit but in later revisions both mandatory consultation and extended time periods are described. In the 2001 Federal Registry there is emphasis placed on a mandatory 120 day consultation. There is no congressional action to date on this FDA recommendation.

WHAT IS MEANT BY "CONSULTATION". AND WHAT ARE ITS GOALS?

The consultation is the term used when a producer of a food product presents to the FDA its intention to bring to market a new or changed food product. The goal is to present to the FDA information in a specific format that confirms that three specific issues are addressed.

- The new food product has not had its safety profile altered or changed by an increase or creation of a new allergen.
- Its toxicity has not been altered.
- Its anti-nutrient profile has not been changed or altered.

Allergenicity: Nearly all known human allergens are proteins. The possibility of introducing an unexpected new protein into the food can and may occur during the genetic engineering process. The process could introduce an unknown allergen into the food or introduce a known allergen into a new food.
Toxicity: Many naturally occurring foods contain small amounts of toxins, but are of such a low level they are in general considered safe. The intention of the FDA is to ensure that the level of toxicity in the bioengineered food does not exceed the level of toxicity in the foods' conventional counterpart. Additionally the FDA is intent on preventing the incorporation of new or unique toxins to the altered food.
Anti-nutrient Effects: Anti-nutrients are naturally occurring compounds that alter or block absorption of nutrients during the digestive process. The FDA is looking to a comparison of the anti-nutrient effects of the new engineered food versus its conventional counterpart. The "Nutrient Profile" of the newly engineered food is also evaluated to measure levels of nutrients equivalent to or greater than the conventional food.

THE CONSULTATION

It is the goal of the consultation, by furnishing relative information to the FDA, that the new bioengineered food product fulfills the above three requirements and more. Once again, one should remember that food producers have the legal responsibility to ensure that their products are safe to consume.

The consulting company presents to the FDA the results of a regimen of test showing the safety of these products. In general, the information provided to the FDA may include, but is not limited to the following information. *From the GAO report.

A. The source of the transferred genetic material, and whether the source of the transferred gene has a history of causing allergic or toxic reactions or has anti-nutrient properties.
B. The degree of similarity between the amino acid sequences in the newly introduced proteins of the bioengineered food and the amino acid sequences in known allergens, toxins and anti-nutrients.
C. Data on in vitro digestibility (ease and completeness of protein breakdown in simulated digestive fluids).
D. The comparative severity of individual allergic reactions to the bioengineered food and its conventional counterpart as measured through blood serum screening. This is performed when the conventional food is known to cause allergic reactions or questions remain about allergenicity.
E. Data on any changes in nutrient substances, such as vitamins, proteins, fats, fiber, starches, sugars, or minerals due to genetic changes from the conventional food.
F. Animal studies as requested by the FDA where deemed necessary or appropriate.

FDA PROCESS AFTER SUBMISSION

The FDA then begins the evaluation process. The average period of time, as stated by FDA records, for completion of evaluation is between 18 months and 3 years. In the initial phase of the consultation the FDA and the applying company review and agree on what specific information will be required for a complete review of the new food. After this the final phase of the process begins. At this point the applying company must supply all information requested and frequently more information and updates as the process proceeds and need for more information is made obvious based on data review. When the FDA process is finished the review, the applicant receives a letter from the FDA stating it has no further questions regarding the safety of the product.

SPECIFICS OF THE PROCESS

"Evaluation of bioengineered food safety submissions must include concurrence from every member of the Biotechnology Evaluation Team". The 1997 guidance (5) states that the evaluation team will be composed of a consumer safety officer (the project manager), molecular biologist, chemist, environmental scientist, toxicologist, and nutritionist. An evaluation team may be supplemented with other experts as need arises. Each member of an evaluation team reviews the ENTIRE FILE. This avoids the concept of a piecemeal evaluation. Each team member receives and examines ALL the data the company submits. Team members must document in writing the results of all key interactions with a company throughout the course of the evaluation. This documentation is available to all members of the evaluation team. Examples of the type of data reviewed by the FDA include, but are not limited to;

- The name of the food and the crop from which it is derived;
- The uses of the food, including both human food and animal feed uses;
- The sources, identities, and functions of introduced genetic material and its stability in the plant;
- The purpose or intended technical effect of the modification and its expected effect on the composition or characteristic properties of the food or feed;
- The identity and function of any new products encoded by the introduced genetic material, including an estimate of its concentration;
- A comparison of the composition or characteristics of the bioengineered food to that of food derived from the parental variety or other commonly consumed varieties with special emphasis on important nutrients, anti-nutrients, and toxicants that occur naturally in the food;
- Information on whether the genetic modification altered the potential for the bioengineered food to induce an allergic response; and
- Other information relevant to the safety and nutritional assessment of the bioengineered food.

FINALLY THE ENTIRE TEAM MUST CONCUR WITH THE FINAL DRAFT OF THE EVLUATION AND ITS POSITON ON THE PRODUCT.

LABELING

"Section 403 of the FD&C Act sets labeling requirements for all foods. All foods, whether derived using bioengineering or not, are subject to these labeling requirements."

"Under section 403(a) (1) of the FD&C Act, a food is misbranded if its labeling is false or misleading in any particular way. Section 201(n) of the FD&C Act provides additional guidance on how labeling may be misleading. It states that labeling is misleading if it fails to reveal all facts that are material in light of such representations (made or suggested in the labeling) or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual."

Although the legislative history of section 201(n) contains little discussion of the word “material,” there is precedent to guide the Agency in its decision regarding whether information on a food is in fact material within the meaning of 201(n). Historically, the FDA has generally limited the scope of the materiality concept to information about the attributes of the food itself. FDA has required special labeling on the basis of it being “material” information in cases where the absence of such information may: pose special health or environmental risks (e.g., warning statement on certain protein diet products); mislead the consumer in light of other statements made on the label (e.g., requirement for quantitative nutrient information when certain nutrient content claims are made about a product); or when consumers may assume that a food, because of its similarity to another food, has nutritional, organoleptic (i.e., affects taste, color, odor, or feel), or functional characteristics of the food it resembles when in fact it does not (e.g., reduced fat margarine may not be suitable for frying).

FDA does not require labeling to indicate whether a food or food ingredient is a bioengineered product, just as it does not require labeling to indicate which conventional breeding technique was used in developing a food plant. Rather, any significant differences in the food itself must be disclosed in labeling. If genetic modifications materially change the composition of a food product, labeling must reflect this. This includes its nutritional content (for example, more oleic acid, or greater content of the amino acid lysine) or requirements for storage, preparation, or cooking, which might impact the food’s safety characteristics or nutritional qualities. For example, one soybean variety was modified to alter the levels of oleic acid in the beans. Because the oil from this soybean is significantly different when compared to conventional soybean oil, the company was advised to adopt a new name for that oil to a name that reflects the intended change.

If a bioengineered food were to contain an allergen not previously found in that food, information about the presence of the allergen would be material as to the potential consequences of consumption of the food. If FDA determined that labeling would be sufficient to enable the food to be safely marketed, the Agency would require that the food be labeled to indicate the presence of the allergen.

FDA has received comments suggesting that foods developed through modern biotechnology should bear a label informing consumers that the food was produced using bioengineering. FDA representatives state they have given careful consideration to these comments. However, they deny having data or other information to form a basis for concluding that the fact that a food (or any of its ingredients) was produced using bioengineering is material within the meaning of 201(n) and, therefore, constitutes information that must be disclosed as part of a bioengineered product’s labeling. Hence, the FDA states that it has neither a scientific nor a legal basis to require such labeling. The FDA has developed, draft guidance for companies who wish voluntarily to label either the presence or absence of bioengineered food in food products.

GAO REVIEW OF THE FDA POLICIES ON GMO

FDA’s overall evaluation process could be enhanced, according to some experts, by randomly verifying the test data that companies provide and by increasing the transparency of the evaluation process—including communicating more clearly the scientific rationale for the agency’s final decision on a GM food safety assessment.

Biotechnology experts from consumer groups and academia state that FDA’s evaluation process could be enhanced if the agency validated companies’ test results on proposed GM products by reviewing raw data (e.g., the actual, unverified test results). Further, FDA believes occasional reviews of the raw data developed by companies would further enhance the credibility of, and public confidence in, the overall safety data that companies submit. In addition, occasional data verification by a federal agency is necessary to identify the risk of the agency's receiving faulty data from external sources and ensure that no one agent is allowed to control every key aspect of a safety assessment.

Officials from a major biotech company described three types of GM food: raw data, refinements and comprehensive interpretations of the raw data, and summaries of these interpretations. According to these officials, FDA has reviewed the summaries, and in some instances the comprehensive interpretations, but has not reviewed the raw data. These officials note, and FDA officials concur, that nothing prevents FDA from reviewing these raw data. In general, these raw data are readily available from companies. Experts from consumer groups and academia have stated that the transparency of the agency's evaluation process for GM could be enhanced if FDA described more clearly the scientific rationale for its safety decisions in its memo to file. FDA agrees. Guidelines issued by the Office of Management and Budget on the quality of information disseminated by federal agencies state that transparency is important in reviews of technical information and that these reviews should be conducted in an open and rigorous manner. Yet critics have stated that FDA's current memos to file do not adequately communicate the scientific rationale for the decisions. Some consumer groups have pointed out the brevity of some of the memos and described them as "perfunctory" summaries of company data that provide little or no insight into FDA's evaluation of the data. Likewise, the Council for Agricultural and Science Technology, a group of universities and companies established to provide a more scientific basis for analyzing and prioritizing agricultural issues, stated that FDA does not adequately clarify in its memos to file the basis for its decisions on GM food submissions. Our review of memos to file for the 50 GM food products evaluated by FDA as of April 2002 confirms that these memos do not clearly explain the scientific rationale for FDA's decisions.

CONSUMER AND ADVOCACY GROUP CONCERNS

The issue of trust both as to WHOM AND WHY NOT is a recurrent issue in literature, international debate and correspondence. The WHOM covers the gamut of U.S. Government agencies including, but not limited to the FDA, USDA, and the EPA all of which are involved in the pre-market review, approval, and post market monitoring of bioengineered (GMO) products. To this list many other international agencies have been added as GM foods have been approved to enter the farms and market places around the world. The other WHOM are the large international corporations that are involved in the creation, production, patenting, and selling of GMO seeds and plant products. Examples of these companies would be Monsanto, Syngenta, Calgene and others. The large international "Agricultural" producers replacing small family farmers such as ConAgra, Cargill, Archer Daniels Midland, and Kraft etc. are also part of the sector accused of lacking credibility in this debate.

The WHY NOT falls into many categories.

A. Most recently the FDA has been found to be slow to act regarding pharmaceuticals with poor safety limits out in the marketplace. The concern is that the FDA is far more stringent in its approval procedure for prescription drugs than it is for foodstuffs. Pharmaceutical approval DOES NOT depend on voluntary consultation but a step-by-step documented and reviewed evaluation. Therefore if the FDA has been shown to be inept on pharmaceutical review, which is complex and in-depth, how can there be any credible controls over GMO food products.

B. An apparent gross conflict of interest between government agencies in place to protect the consumers, and corporations dependent on acceptance and market success for its products. Advocacy groups point out that there is an "apparent revolving door" at both the middle and upper management levels between the government agencies and private industries. Directors of the USDA and FDA often come from the large firms described above, or go from government agencies to boards or directorships of the large companies they have regulated in the past. Although these appointments are transparent and are public information it does create a deep sense of distrust.

C. An over-weighted dependence by government agencies on data supplied by private industry with an interest in a positive out come of the studies. This coupled with an admitted (by the FDA) lack of review of submitted raw data is an area many groups find unacceptable.
D. Both the concept of "substantial equivalence" and GRAS (generally accepted as safe) are difficult to grasp as to their application to GMO. Below are two definitions of these concepts as put forth by the FDA and the Biotechnology industry.

GRAS

"GRAS" is an acronym for the phrase **G**enerally **R**ecognized **A**s **S**afe. Under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act (the Act), any substance that is intentionally added to food is a food additive, that is subject to pre-market review and approval by FDA, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use, or unless the use of the substance is otherwise excluded from the definition of a food additive. For example, substances whose use meets the definition of a pesticide, a dietary ingredient of a dietary supplement, a color additive, a new animal drug, or a substance approved for such use prior to September 6, 1958, are excluded from the definition of food additive. Sections 201(s) and 409 were enacted in 1958 as part of the Food Additives Amendment to the Act. While it is impracticable to list all ingredients whose use is generally recognized as safe, FDA published a partial list of food ingredients whose use is generally recognized as safe to aid the industry's understanding of what did not require approval. Under sections 201(s) and 409 of the Act, and FDA's implementing regulations in 21 CFR 170.3 and 21 CFR 170.30, the use of a food substance may be GRAS either through scientific procedures or, for a substance used in food before 1958, through experience based on common use in food.

Under 21 CFR 170.30(b), general recognition of safety through scientific procedures requires the same quantity and quality of scientific evidence as is required to obtain approval of the substance as a food additive and ordinarily is based upon published studies, which may be corroborated by unpublished studies and other data and information.

Under 21 CFR 170.30(c) and 170.3(f), general recognition of safety through experience based on common use in foods requires a substantial history of consumption for food use by a significant number of consumers. Regardless of whether the use of a substance is a food additive use or is GRAS, there must be evidence that the substance is safe under the conditions of its intended use. FDA has defined "safe" (21 CFR 170.3(i)) as a reasonable certainty in the minds of competent scientists that the substance is not harmful under its intended conditions of use. The specific data and information that demonstrate safety depend on the characteristics of the substance, the estimated dietary intake, and the population that will consume the substance. A GRAS substance is distinguished from a food additive on the basis of the common knowledge about the safety of the substance for its intended use. As FDA discussed in a proposed rule to establish a voluntary notification program for GRAS substances (62 Fed. Reg. 18938; April 17, 1997), the data and information relied on to establish the safety of the use of a GRAS substance must be generally available (e.g., through publication in the scientific literature) and there must be a basis to conclude that there is consensus among qualified experts about the safety of the substance for its intended use. Thus, the difference between use of a food additive and use of a GRAS substance relates to the widespread awareness of the data and information about the substance, i.e., who has access to the data and information and who has reviewed those data and information.

A. For a food additive, privately held data and information about the use of the substance are sent by the sponsor to FDA and FDA evaluates those data and information to determine whether they establish that the substance is safe under the conditions of its intended use (21 CFR 171.1). Concerned consumers point out the passive, dependent position of the FDA on data presented by the developer. Generally there is no review of raw data by the FDA. Transparency is poor as the data is often presented as proprietary and not available for public scrutiny or peer review.

B. For a GRAS substance, generally available data and information about the use of the substance are known and accepted widely by qualified experts, and there is a basis to conclude that there is consensus among qualified experts that those data and information establish that the substance is safe under the conditions of its intended use. (proposed 170.36 (c)(4)(i)(C))

SUBSTANTIAL EQUIVALENCE

Guiding this assessment is the concept of "substantial equivalence," which was introduced by the Organization for Economic Cooperation and Development in 1993. Substantial equivalence is widely regarded as a sound basis for safeguarding the quality and safety of biotech foods and provides an historical context based on centuries of experience with conventional foods. In addition to the OECD, this standard has been validated by many international scientific and governmental organizations, including the U.N. Food and Agriculture Organization and World Health Organization and the International Life Science Institute. The FDA's 1992 Statement on Policy on biotech foods, which lays out the agency's approach to biotech regulation, is consistent with substantial equivalence, and many other government regulatory agencies also have adopted it in their regulatory reviews.

Stated simply, substantial equivalence holds that a biotech food is as safe to consume as an existing food with the same compositional and nutritional characteristics and a history of safe use. The main food-safety issues for biotech varieties crops are changes in allergenicity, toxicity, nutrient composition and level, unintended effects, and the safety of antibiotic-resistant marker-encoded proteins included with the transgene. This evaluation seeks to establish that the new varieties are as safe as or safer than crops produced by traditional methods.

Evaluating the substantial equivalence of a new food involves measuring the bioavailability and concentration of important nutrients in the food-such as proteins, carbohydrates, vitamins, minerals, fats and oils-to ensure that they fall within the normal range of variability for the food. As many foods contain naturally occurring toxins and anti-nutrients, levels of these substances also are tested and compared. Immunological testing also is conducted. In contrast, there are relatively few analytical studies done on conventional varieties of crops during development.

Substantial equivalence is not the end of the safety assessment, but the beginning. The results of these analyses can yield three conclusions. The new food may be found: 1) substantially equivalent to a conventional counterpart; 2) substantially equivalent except for a few clearly defined differences; and 3) not substantially equivalent. Any significant differences between the biotech food and its conventional counterpart would trigger additional tests and mandatory labeling.

Regardless of these definitions, consumer and advocacy groups feel strongly that the above definitions DO NOT represent the possibility of safety problems with genes inserted into DNA that is not consistent with the original organism. It is their contention that a modified organism does not represent any form of equivalence to the conventional food to which it is compared.

USE OF INDUSTRY STUDIES WITHOUT TRANSPARENCY

It is the feeling of advocacy groups that studies, particularly short term feeding studies, are not available for peer-reviewed evaluation because of the proprietary nature of the data. Large industry prepares studies including raw data and assumptions made to come to a conclusion. By the nature of the final study being classified by industry as proprietary in nature third party neutral peer review cannot be conducted.

Advocacy groups deem results of such short and intermediate feeding studies as both absolutely necessary and available prior to the release of a new GM food product.

LONG TERM AND MULTIGENERATIONAL FEEDING STUDIES

One of the most heated issues in this debate relates to long term and multigenerational feeding studies. Advocacy and consumer groups feel that the “Precautionary Principal” is the best approach with GM foods. At the center of the precautionary principle is the concept of taking anticipatory action in the absence of complete proof of harm, particularly when there is scientific uncertainty about causal links (Jackson, 1993). The precautionary principle states that decision makers should act in advance of scientific certainty to prevent harm to humans and the environment (O'Riordan and Jordan, 1995). It addresses many of the limitations of current decision-making methods, problems of cumulative effects, and limitations of science. The ancient concept of medicine “First Do No Harm” is the simplified concept. Biotechnology advocates take a different view of both the value of long term and multigenerational studies. Scientists and federal regulatory officials generally agreed that long-term monitoring of the human health risks of GM food through epidemiological studies is not necessary because there is no scientific evidence suggesting any long-term harm from these foods. These scientists also stated that it would be very difficult, if not impossible, to develop a process for monitoring the long-term health risks of GM foods because of the technical challenges in developing such a system. A recent report by the United Nations also expresses skepticism about the feasibility of identifying long-term health effects from GM foods. The scientists and federal regulatory officials generally agreed that because there is no scientific evidence that GM foods cause long-term harm, such as increased cancer rates, there is no plausible hypothesis of harm. Researchers need such a hypothesis in order to know what problem to search for, test, and potentially measure. The biotechnology industry also has concerns that the essence of the “precautionary principle” is misused and its application by advocates is to treat a lack of evidence as evidence against bringing out new GM foods.

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Standardization of Testing Protocols and Compliance Review

As the technology was being developed, scientists, regulators and policymakers agreed that crops developed by recombinant biotechnology should be evaluated before release to widespread use, and therefore, the *Coordinated Framework for Regulation of Biotechnology* was published under the auspices of the White House Office of Science and Technology in June, 1986 (CAST, 2001). This gave responsibility of implementation of the Framework to three federal agencies:

1. *United States Department of Agriculture (USDA):* specifically APHIS (Animal and Plant Health Inspection Service is responsible for environmental safety under the authority of the Plant Protection Act (PPA) and the National Environmental Policy Act (NEPA) which gives APHIS the authority to regulate the movement, import, and release of plant pests or potential plant pests. APHIS basically assesses whether a new crop developed by biotechnology will become a weed, create a pest by outcrossing or otherwise have adverse impacts on environment or agriculture.

2. *Food and Drug Administration (FDA):* as discussed above, FDA is granted primary authority for the safety of food by the Federal Food, Drug, and Cosmetic Act (FFDCA), which stipulates that food safety be defined by a reasonable certainty of no harm.
3. *Environmental Protection Agency (EPA):* regulates pesticides produced by genetically modified plants under the authority of the Federal Insecticide Fungicide, and Rodenticide Act (FIFRA) for plant incorporated protectants (PIP). Any genetic modification that expresses a protein that resists a pest or disease falls under EPA regulation for sale, distribution and use as a pesticide (EPA, 2001)

REGULATORY PROCESS

The general regulatory process is described in CAST (2001), National Research Council (2000), APHIS (2002), Thomas and Fuchs (2002), and McHughen (2000). Essentially, there are nine steps in the U.S. governmental safety evaluation of food and agricultural products developed using recombinant biotechnology:

1. *Biosafety Committee—National Institutes of Health Biosafety Guidelines (required for institutions receiving federal funding)**
2. *USDA greenhouse standards and inspection*
3. *USDA field trial authorization*
4. *USDA authorization of transport for field trials*
5. *USDA determination of nonregulated status**
6. *EPA experimental use permit approval**
7. *EPA determination of food tolerance or tolerance exemption**
8. *EPA product registration**
9. *FDA review process (voluntary premarket consultation)—this step has been reviewed in the section above and has the most direct impact on human health.*

SAFETY ASSESSMENT OF TRANSGENIC CROPS

The key requirements for U.S. safety assessments of new transgenic crops that have the most significant implications on human health and are assessed by EPA, USDA, and FDA:

1. *product description: data on host and parent plant, introduced or novel genetic material and intended effect of introduced gene.*
2. *molecular characterization: location of inserted gene in genome*
3. *toxicity studies: tests demonstrating safety of transgenic protein*
4. *nutritional data: analyses over several seasons and locations*
5. *substantial equivalency: data proving that transgenic is different from non-biotech variety by only the intended transgenic effect*
6. *allergenicity: analyses that transgenic protein is unlikely to cause allergies in humans*
7. *natural toxicants: analyses showing no increase in natural toxicants*
8. *environmental impact: studies showing that biotech variety is unlikely to have adverse effects in terms of: outcrossing and gene flow to wild relatives, and any effect on plant's ability to reproduce in wild*

REVISING REGULATIONS

There have been calls to revamp the regulatory process to more of a case by case basis so that the public sector (i.e.universities) can become more compelled to delve into the discovery stages: (Bradford et al. 2005). Scientists are proposing that regulatory emphasis should be put on phenotypic (the plant's properties) rather than genomic (DNA) characteristics once a gene has been shown to be safe. Scientists have called for a greater discrimination in how regulations are applied rather than a blanket process which clearly is not warranted for certain categories of transgenic events (Strauss, 2003 (a); Hancock, 2003; Straus 2003 (b)) Indiscriminant regulation confuses the public regarding the risk and novelty, inflaming rather than resolving the debate over transgenic foods.

Risk categories proposed (Bradford et al. 2005) are:

1. Low risk with reduced regulatory oversight: where imparted traits are functionally equivalent and no novel biochemical or enzymatic functions are imparted (that is the plant is not materially changed)—where genetic engineering brings about directed changes in expression of functionally homologous genes to obtain a commercially useful trait. National Research Council suggests there are many transgenic traits that should not be subject to bioconfinement
2. moderate risk: the plants make pharmaceutical/industrial proteins or plants with novel proteins that have very low toxicity to humans and environment
3. high risk: heavily regulate transgenic plants that have or produce proteins that have a documented likelihood of harming humans or the environment

SCIENTIFICALLY BASED CONCERNS

Transgenic events that should warrant more stringent regulation should be for crop species where close relatives might be grown nearby and these decisions should be based on the biology of the plant (e.g. outcrosser (caution) vs. selfer (not alarming)) these cases should be based on the assessment of plant biologists (Ellstrand et al., 1999; Stewart et al. 2003). In response to public concern and criticisms by the National Academy of Science, the USDA is revising its oversight of "pharma" and "industrial" crops. These are transgenic crops that are genetically modified to produce pharmaceutical or industrial products. Concern remains among scientists that these transgenic events should not be pursued when the parent line is a food crop (Gurian-Sherman, 2003; Strauss, 2003).

General Distrust of Transgenic Science

PUSZTAI DEBACLE

Considerable attention has been given to isolated cases. Very often the book, 'Seeds of Deception" written by Jeffery Smith (2003) who is, by his own admission is not a scientist, has been cited as a legitimate reference calling for the banning or restriction of genetically modified foods. The first portion of that book is dedicated to a description of the deconstruction of the career of Arpad Pusztai following the publication of his and Stanley Ewen's paper, 'Effect of diets containing genetically modified potatoes expressing Galanthus lectin on rat small intestine'' in the British medical journal, The Lancet. This study does lead to questions as to whether the effects of snowdrop lectin (*Galanthus nivalis* agglutintin, GNA) on morphological alterations of rat intestines had been accentuated in genetically modified potatoes. We are not aware of any replication of the 6 rat per treatment, 10 day study. Criticisms include the lack of a control by not having a blank vector, that the high sources of variation may be due to archaic formalin- fixation image analysis methods, that the gut lesions reported were smaller than normally reported further bring this study to question, that intraepithelial lymphocyte counts were not done by a well established method, that increased lymphocyte counts within normal ranges without proper control groups. (Mowat, 1999; FitzGerald et al. 1999; Lachman, 1999; Kuiper et al. 1999). Plant molecular biologists have added to further criticisms that Ewen and Pusztai's (1999) observations were the result of effects due to somaclonal variation and not due to the transgenic process *per se* (Federoff and Brown, 2004; McHughen, 2000). Somaclonal variation is a common problem when growing out a newly genetically transformed plant cell on tissue culture because of the changes due to random mutation and the extremely narrow genetic variation experienced when starting from a single cell. The resulting transgenic plant can be very different from the original parent line. These differences are not restricted to the inserted transgene but often extend to the entire genome. In an attempt to rectify this issue, members of this panel (Steinmaus and Broadhurst) attempted to assess Pusztai's claims directly. Pusztai's response to the question "how did you transform the GM potatoes used in your experiments" Pusztai replied, "…internodal stem fragment propagation…", which indicates that he did not perform the original transformation event, does not know about the original transformation event, or will not tell us about the original transformation event (Steinmaus, pers. comm..). There were no additional exchanges. Additionally, in the same section of Research Letters a letter from Fenton et al. (1999) proclaims that snowdrop lectin (GNA), the same protein that Ewen and Pusztai reported on, shows a propensity to bind to human white blood cells thus calling for a greater understanding of this source of lectin before placing it into the human food chain. The publication of these two papers back to back in the same issue of The Lancet demonstrates the scientific method at work. It is doubtful that snowdrop lectin (GNA) will ever see the light of day in a grocery store without further serious scrutiny. After studying the evidence and listening to testimony, a British Royal Society commission reported that no scientifically meaningful conclusion could be reached from Ewen and Pusztai's (1999) experiments.

SHOWA DENKO L-TRYPTOPHAN

Additional attention was given to Smith's coverage of ShowaDenko's tryptophan toxicity episode that resulted in some deaths and illnesses and how this was tied to the transgenic process. In actuality: the toxic contaminant in the dietary supplements was found to be the result of an elimination of a key purification process and NOT from the bacteria being genetically engineered (Beachy et al., 2002; Avery, 2002). Further, some have attributed the toxic effects, such as eosinophilia-myalgia syndrome, to the consumption of unprecedented high doses of L-tryptophan per se (FDA, 2001).

RANDOM TRANSGENIC INSERTION

Concerns have been expressed regarding effects of randomly introduced genes. When referring to the technique by which cloned genes are inserted into genome via the biolistics or any cloning vector technique: this is where screening and selection comes in. Inverse PCR and sequencing of adjacent DNA identifies where transgenes have been inserted into a host genome. If the transgene disrupts important genes the cells will not survive. Further testing of expression determines whether pleiotropic effects make the transgenic product substantially equivalent or not. The proof of 'substantial equivalence' is the best tool science has to demonstrate safety for something that can never be proven completely safe regardless of the production technology. International consensus has been reached regarding the assessment of food safety of genetically modified plants and the concept of substantial equivalence is the framework of choice (Kuiper et al., 2001). However, it should be noted that further assessment methods such as DNA microarray, proteomics, and metabolomics for the identification of unintended effects should be pursued as recommended in the National Academy of Sciences (2004) discussed in the following sections.

UNEXPECTED VIRULENCE

In reference to unintended effects due to changes in the genome and fusion proteins, an example is a case that surprised molecular biologists at first. Creation of a mousepox virus unexpectedly became more virulent in mice when Australian researchers introduced an interleukin-4 gene (Jackson et al., 2001). However, the creation the killer poxvirus was predictable and not surprising as interleukin-4 is known to potentiate immunogenicity (Mullbacher and Lobigs, 2001). Given this evidence, the general consensus among biotechnologists is that the paper underlines the fact that no technology is risk-free but by no means should the possibility of unexpected consequences such as these cause us to abandon the technology (Editors, 2002).

PLEIOTROPIC EFFECTS

The task force heard a presentation of arguments from the public listed in Schubert (2002):

- Introduced gene may produce different proteins in different cell types.
- Introduced gene may produce proteins that will react with other substances in the cell resulting in molecules that are toxic, allergenic or carcinogenic.
- Introduced gene may result in formation of a new biochemical pathway that will produce unexpected products of physiological consequence.

The counter argument is that these scenarios all arise in the course of evolution and are unlikely to pass the screening cascade to which all new crops are subjected (Beachy et al. 2002; Avery, 2002). It is acknowledged that Schubert has identified the problems that may possibly occur. However, they are all predictions. Secondly, biotech crops are subjected to a battery of tests designed to detect unpredicted effects from many kinds of sources including alternative splicing of mRNAs and post-translational processing of target proteins and any other unintended impacts of on plant metabolism that may occur. The fundamental flaw in Schubert's logic is that his stated concerns already occur in nature as a consequence of mutation and other rearrangements (e.g. transposons) and that they are subjected to the perils of natural selection. Further, all forms of breeding including conventional (and sometimes, especially conventional) have the potential to produce different proteins in different cell types or produce substances that could be harmful (Fu and Dooner, 2002). To dismiss completely the idea that biotechnology is very similar to classical plant breeding (except that it is more precise) contributes to the deconstruction of Schubert's conclusions by Beachy et al (2002) and Avery (2002).

Allegenicity, Unintended Effects and Antibiotic Markers

ASSESSING ALLERGENICITY

The subject of allergenicity is referenced in several other sections of this report. Just to summarize the issue, a joint panel of experts from the International Life Science Institute and International Food Biotechnology Council developed the first detailed scheme for assessing food allergenicity (Metcalfe et al., 1996) which was revised by another expert panel held by the Food and Agricultural Organization (FAO)/World Health Organization (WHO) in 200. The scheme emphasizes looking at the source of the new gene, the amount of amino acid similarity shared with known allergens, the expression level of the protein in the biotechnology derived crop, the function of the novel protein, the reactivity of the protein with IgE antibodies from the serum of individuals having known allergies to the source of the transferred genetic material, and the sensitivity of the new protein to heat and digestion. Most food allergens are proteins that are at least partially resistant to digestion or food processing and the subject of the rapidly evolving field of allergenicity (Chassy, 2002).

BRAZIL-NUT GENE

This issue was brought up during public comment referring to the case when researchers introduced brazil-nut genes into soybean. The transgene of concern was brazil-nut albumin, which was engineered into soybean to increase methionine content. The researchers found that serum from brazil-nut allergic people reacted with extracts of the transgenic soybean and not to untransformed soybean. This became apparent to Pioneer Hi-Bred International during their safety testing and they agreed with FDA that the product should not be commercialized and it never reached market.

DETECTING AND REMOVING ALLERGENS

Breiteneder and Mills (2005) indicate that the dominating plant food allergen groups belong to a few superfamilies: promalin, cupin and the Bet v 1 family of allergens. They have been well characterized. Transgenic expression of proteins within these protein superfamilies can be detected and their presence in foods anticipated. Thomas and Fuchs (2002) provide compelling evidence and argument for the power of biotechnology to actually remove or reduce allergens from common foods.

HORIZONTAL GENE TRANSFER

Fear of inadvertent gene transfer directly from consumption of GM foods or indirectly from consuming animals fed GM feed to the human gut were expressed at one task force meeting. Netherwood et al. (2004) found low frequency gene transfer from GM soybean to the microflora of the small bowel of human subjects with ileostomies prior to their involvement in the feeding study but no increase in gene transfer during the study. Transgenes survived digestion at low rates in the ileostomists but not in the intact gastrointestinal tract of control subjects. Thus this is of minor concern for humans with intact gastrointestinal tracts directly consuming transgenes from plants. It is even less concerning for humans consuming meat raised on transgenic food as the transgenes would have to survive digestion by two animal gastrointestinal tracts.

SELECTABLE ANTIBIOTIC MARKERS

Selectable antibiotic resistance markers are commonly used during the development of GMO's. Recent publications emphasize that horizontal gene transfer from transgenic plants to soil bacteria should be monitored (Nielsen and Townsend 2004) even though it is unlikely due to significant biological hurdles (Davison, 2004). The AMA recommends not using antibiotic markers if avoidable while recognizing the relative low risk of such screening methods (AMA, 2000) The potential for horizontal gene transfer from GM food to human gut microbes in humans with impaired gastrointestinal tracts (Netherwood et al. 2004) might detract from public acceptance if the public did not understand the nature of the transfer. Two strategies exist to improve public acceptance of GM foods in this regard:

1. Produce marker-free plants by removing the marker using site specific recombination, transposon-mediated elimination or cotransformation followed by segregation. Some GM plants do not require an antibiotic marker because the transgene itself is a selectable marker, for example, the modified EPSPS in Roundup Ready crop varieties can be selected in media laced with glyphosate (Roundup).
2. Often it's more efficient to leave the marker in the plant but to use a plant-based marker. This can be done using plant genes, regulatory elements, T-DNA borders-like sequences, and selectable markers originating from plants. Herbicide tolerant plants already possess a selectable plant based marker---the herbicide tolerance. The recent discovery of the

Atwbc19 marker which uses the plant's own genome to confer kanamycin resistance, which is the most commonly used GM antibiotic marker (Mentewab and Stewart, 2005).

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Nutrition and GMOs

INTRODUCTION

Nutritional aspects of genetically engineered (GE) foods are important, since nutrition is one area which can impact virtually all people. By far, most GE foods in terms of acres planted, harvested, and processed as food have been developed to aid the grower in reducing production costs associated with pest management. Some GE foods are being developed to improve the nutritional quality of that food (*e.g.* "golden" rice and soy with higher quality protein). When the reason for the GE is not nutritionally related, there is still the possibility that the nutritional quality of the food may be affected, or even that the modified food could be toxic to humans. Clearly, the nutritional quality of GE foods must be verified. We note that American Dietary Association (ADA) has recently endorsed GE crops (ADA, 2006)

<u>DIFFICULTIES IN NUTRITIONAL TESTING</u>

Nutritional studies have always been difficult. Proper control populations may be difficult to define, genetic individuality within test populations may obscure the results, animal testing is not always comparable to using human subjects and informed consent considerations limit the conditions under which the tests can be performed (tests using prisoners, graduate students and conscientious objectors are often banned or limited in ways which were not true in the past).

One aspect of nutrition that complicates the research is the long time it takes for minor changes in nutritional quality to show up. For example, bleached flour was developed before the existence of vitamins was understood; now we use fortified white flour. The potential problems of *trans*-fatty acids are just beginning to come to light. It may be impossible to determine such long-term effects of *minor* changes in nutrient levels. Within a balanced diet, nutritional effects of small amounts of GE foods may be impossible to detect, and it may take many generations to ascertain those effects. ["Pottenger's Cats" tells an interesting story about generations of cats on abnormal diets. (Pottenger, 1933)]

If one looks only at modified foods created through traditional methods, such as selective breeding, and irradiation to create mutations large changes in nutritional quality may be easy to determine, but small changes may not be so obvious. Certain families (e.g. Solanaceae, the nightshade family which includes potato, tomato, and tobacco) contain known toxins which have increased, on occasion, in varieties created through traditional methods, so new varieties of all types should tested.

There is <u>no</u> natural food for which we know <u>every</u> ingredient. In fact, we may only know a small percentage of a food's components. Few "natural" foods have been tested for their safety. GE foods add additional concerns, since genes from different families or even different phyla or kingdoms may be involved (e.g. bacterial genes or genes modified in the lab). These foreign genes may produce a product which is known to be safe, but we do not know what or if additional effects may have been introduced.

EXTENT OF CURRENT RESEARCH

Nutritional testing of GE foods has been minimal and results have not been consistent about safety. For example, Roundup-Ready® (glyphosate tolerant) crops and the foods derived from them have been shown to be safe, the protein is digested and nutritional value to animals is not affected (Hammond, Harrison), although some have questioned this determination. A lectin-rich potato resulted in lesions in the digestive tract in tested rats (Pusztai, 1999), but the study did not include appropriate controls and it was not clear that genetic modification caused the problem.

Other studies have suggested allergenicity (Brazil nut genes), reduced digestibility (due to lignin) and transfer of fragments of genes (Roundup-Ready® and most likely many others) to intestinal bacteria (Netherwood, 2004). An allergic reaction could be easily shown to be due to the nature of the added gene (Nordlee, 1996), not due to the GE modification method, *per se.* Increased lignin production may have been due to the method, since a bacterial gene was added, not a lignin gene (Jung, 2004). New genetic methods for gene transfer are being developed to solve the third problem. Sometimes, a gene for a GE protein produces a slightly modified protein, which can be allergenic (Prescott, 2005).

Awareness of these problems causes scientists to refine and modify their methods, developing better and more precise methods of gene delivery, altering the cloning techniques to maintain the exact sequences in the origin genes and the product proteins and developing safer and more subtle methods for subsequent detection of new genes. Furthermore, a problem such as lesions or bleeding due to ingestion of a GE crop *will* prevent that crop from ever entering the commercial market. Thus, one could argue that appropriate testing methods currently in use may be adequate to identify problems.

WHAT NUTRITIONAL TESTING CAN OR MIGHT BE REQUIRED?

There are several levels of possibility:

- Is the new variety truly “substantially equivalent”; in that GLP (Good Laboratory Practices, the accepted standard) do not indicate any differences?
- Is there any difference due to the new gene product?
- Has some other gene product been affected
- Has the genetic modification been incorporated into the genome of the consumer of the food; or more likely into the subject’s intestinal flora?

Two questions arise. 1) How do you look for an unknown something, which may or may not exist? 2) How do you prove something is 100% safe? Neither question has an obvious practical answer. Recommendations must be within practical levels. The necessary testing depends on the type of genetic modification, on a case-by-case basis. Based on our studies and experience, any suggested testing would apply to all GE foods and are not specific to SLO County.

The extent of testing would likely depend on the extent of genetic difference between the source and recipient species. The testing bar gets higher as the donor genes and recipient species get further apart. Crossing legumes or grains may be considered to be inherently less risky than adding bacterial or animal genes to crops. Potential allergic substances could be especially problematic [*e.g.* shrimp pigments or fish antifreeze genes in strawberries and nut genes in soy (Nordlee, 1996)]. Again, appropriate labeling seems a given, since the FDA has begun requiring labels to specify potential allergens, even to the extent of saying “*may* contain the following allergens” or “has been exposed to equipment used with the following allergens.”

OTHER CONCERNS

Suggestions to add vaccines or pharmaceuticals into foods will involve testing similar to those listed previously, with the added caveat that the vaccine must have its safety and efficacy tested as well, following FDA guidelines.

Suggestions to increase the content of nutrients, such as vitamin A or precursors, must increase these nutrients to effective levels. Golden rice may not have adequate amounts to make it an effective source of vitamin A, especially in children. The nutrient must also be proven to be in a form, which is readily absorbed, or it will not be effective. The natural matrix of the food may need to be undisturbed to assure that absorption occurs. These facts can be easily determined using current methods.

SPECIFIC CONCERNS FOR SLO COUNTY

Since commercial food, especially processed and blended food, comes from all over the USA and the world, nutritional concerns about GE foods grown in SLO County may be moot. However, nutritional education is an issue we *must* address. There is a general need for more nutritional “literacy” among Americans (not just SLO) and for them to apply this knowledge to their diet and life-style. For example, Nepal and Thailand have been able to alleviate vitamin A deficiency through education about eating more diverse diets (Katmandu, 1981; UNICEF, 1993; DeCava, 2004, Thailand, 2006). New foods were added to their diets, rather than depending on genetically modified golden rice.

Clearly, more knowledge about nutrition, coupled with application of that knowledge, would benefit SLO citizens. The nature of such education should include awareness of problems with *all* foods, not just GE varieties. Working with the Education Committee of the Health Commission, nutritional information about GE foods could be integrated with other topics, pamphlets could be produced and a cluster of public speakers able to address these issues could be established.

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National Academy of Sciences Report

The National Academy of Sciences (NAS) report is a document commissioned by the FDA, EPA, and USDA. Entitled, ‘Safety of Genetically Engineered Foods, Approaches to Assessing Unintended Health Effects, the report was published in July, 2004 in an effort to compile recommendations for improved procedures to ensure new genetically modified foods that reach the market have had a thorough assessment. This assessment focuses on procedures to mitigate possible unintended effects that might occur because of compositional changes in the new food when compared to its origins.

First, it is important to note one main conclusion from the report that unintended health effects are possible when new foods are introduced regardless of their method of genetic modification. For example, Kiwi fruit was introduced in the last century as a result of conventional breeding. Once marketed, Kiwi was found to cause allergenic reactions in a few people that were severe enough to cause death in some cases.

The recommendations from the NAS report take a rather global approach to dealing with possible unintended effects arising from genetically modified crops. As such, these recommendations do not overlay clearly with the needs and more specific issues facing the citizens of SLO County. Nonetheless for many of these issues, the recommendations provide considerable insight into how to develop more SLO County-specific guidelines for assessing possible adverse unintended effects related to the health of our citizens.

Following are the recommendations 1 through 5. These have particular relevance to issues that appear of concern for SLO County.

Recommendation 1: “The committee recommends that compositional changes that result from all genetic modification in food, including genetic engineering, undergo an appropriate safety assessment. The extent of an appropriate safety assessment should be determined prior to commercialization. It should be based on the presence of novel compounds or substantial changes in the levels of naturally occurring substances, such as nutrients that are above or below the normal range for that species, taking into account the organism modified and the nature of the introduced trait.”

Recommendation 2: “The committee recommends that the appropriate federal agencies determine if evaluation of a new GM foods for potential adverse health effects from both intended and unintended compositional changes is warranted by elevated concern, such as identification of a novel substance or levels of a naturally occurring substance that exceeds the range of recommended or tolerable intake.”

Recommendation 3: “For those foods warranting further evaluation, the committee recommends that a safety assessment should be conducted prior to commercialization and continued evaluation post-market where safety concerns are present. Specifically, the committee recommends the following safety assessment actions:

- Develop a paradigm for identifying appropriate comparators for GE food.
- Collect and make publicly available key compositional information on essential nutrients, known toxicants, antinutrients and allergens of commonly consumed varieties of food. These should include mean values and ranges that typically occur as a function of genetic makeup, differences in physiological state and environmental variables.
- Remove compositional information on GE foods from proprietary domains to improve public accessibility.

- o Continue appropriate safe assessments after commercialization to verify pre-market evaluations, particularly if the novelty of the introduced substance of the level of a naturally occurring substance leads to increased safety concerns."

Recommendation #4: "The committee recommends the development and employment of standardized sampling methodologies, validation procedures and performance-based techniques for target analyses and profiling of GM food ..Sampling methodology should include suitable comparisons to the near isogenic parental variety of a species grown under a variety of environmental conditions, as well as ongoing assessment of commonly consumed commercial varieties of food…"

Recommendation #5: When warranted by changes such as altered levels of naturally occurring components above those found in the product's unmodified counterpart, population-specific vulnerabilities, or unexplained clusters of adverse health effects, the committee recommends improving the tracking of potential health consequences from commercially available foods that are genetically modified, including those that are genetically engineered…"

In the detail below recommendations from the NAS report are matched with issues that have emerged during the task force work and include descriptive phrases from the relevant recommendation.

Government Regulations, Laws and Standards

- Much call for labeling. *Compositional changes found and assessed under recommendations 1-3 could trigger labeling under existing FDA guidelines and follow-up surveillance under recommendation 5.*
- Standardization of testing protocols and compliance review – *Recommendation 3.*
- Risk Assessment vs. precautionary – *Recommendation 4 (Reevaluation of current methodologies… and use of data collection programs… currently available…tools are inadequate for correlating compositional analyses with biological effects) and recommendation 5 (post market surveillance).*
- Phenotypic vs. genomic characterization – *Recommendation 2 (…assessment of foods based on method unjustified…)*

Transgenic Science

- Surrogate proteins for testing – *Recommendation 4 (…standardized…profiling of GM food…and recommendation 5 (Develop a database of unique genetic sequences…).*
- Effects of randomly introduced genes and powerful regulatory elements – *Recommendation 2 (novel substances or levels trigger evaluation for potential adverse effects) and recommendation 3 (safety assessment prior to commercialization based on standard paradigm).*
- Unintended effects due to changes in the genome and fusion proteins – *Recommendation 1 (The committee recommends that compositional changes that result from all genetic modification in food…undergo an appropriate safety assessment) and recommendation 2-4 (methods).*
- Schubert arguments - *Recommendation 1 (The committee recommends that compositional changes that result from all genetic modification in food…undergo an appropriate safety assessment) and recommendation 2-4 (methods). Recommendation 2 (Introduction of novel components into food through genetic engineering can pose unique problems…)*

The Scientific Method

- The public lacks perspective to assess whether something should be considered dangerous – *When adopted, the NAS recommendations provide a structured system for assessing unintended effects of* *genetic modification. With public education, confidence should be increased in the public for the agencies ability to regulate the introduction of new foods.*

- The scientific method allows assessments of hazards based in evidence, not prediction. The public does not appreciate the power of this method. - *Recommendation 1 (The committee recommends that compositional changes that result from all genetic modification in food…undergo an appropriate safety assessment) and recommendation 2-4 (methods).*
- The scientific method ensures that all likely consequences of an experiment are evaluated in a logical and systematic fashion. Events are not taken at face value, rather possible outcomes are evaluated. *Recommendation 4.*
- Attention to isolated information can instill fear. - *If adopted, the NAS recommendations provide a structured system for assessing unintended effects of genetic modification. With public education, confidence should be increased in the public for the agencies ability to regulate the introduction of new foods.*
- Proof of 'substantial equivalence' is the tool science uses to demonstrate safety when absolute safety cannot be proven. - *Recommendation 1 (The committee recommends that compositional changes that result from all genetic modification in food…undergo an appropriate safety assessment).*

Allergic Reactions

- Concern that allergic reactions will be elicited by the technology – *Recommendation 4 (…reassess the biological consequences of unintended changes in GM food…using…better tools… …collect information to identify food consumption patterns in the general population and susceptible…subgroups…) and recommendation 5 (Improve the ability to identify populations that are susceptible to food allergens and develop…)*
- Known foods containing allergens (marketed for decades) are labeled – *See the FDA guidelines for labeling foods in the section on FDA.*
- Some GM foods have removed allergenic problems, e.g. soybeans – *The NAS recommendation 4 would strengthen the ability to assess allergen content and predict impacts on the general population.*
- The few plant food allergen groups are well understood. They can be detected in new foods – *Recommendation 4 (The committee recommends the development and employment of standardized sampling methodologies…for targeted analyses and profiling of GM food…)*

GMO in foods

- Unintended effects - *Recommendation 1 (The committee recommends that compositional changes that result from all genetic modification in food…undergo an appropriate safety assessment) and recommendation 2-4 (methods).*
- Contamination of food crops destined to produce non-foods, e.g. pharmaceuticals or plastics. – *Not specifically addressed by NAS report.*
- Lack of chronic toxicity testing – *Recommendation 5 (post market surveillance) and recommendation 1 (The committee recommends that compositional changes…undergo appropriate safety assessment…the extent of which…should be determined prior to commercialization.)*
- EU has embraced the precautionary principle & set labeling thresholds. *See the discussion of the Precautionary Principle.*
- Several other regions have shown concern and/or not allowed GMO imports from the US – *Perhaps the applications of recommendation 1-5 will improved the confidence world-wide in the safety of GM foods.*

Children

- They may be more susceptible to any unknown effects - *Recommendation 4 (…reassess the biological consequences of unintended changes in GM food…using…better tools… …collect information to identify food consumption patterns in the general population and susceptible…subgroups…).*

There are a few other issues that emerged that may or may not match up well with the NAS recommendations. I have picked the ones that I feel are most important to discuss here.

Two main traits dominate current production of GM crops both in the US and other parts of the world. Roundup Ready uses a bacterial gene to make the crop tolerant of being sprayed with the herbicide Roundup. Main existing crops exhibiting this trait are soybeans, corn and cotton. Other crops such as alfalfa are beginning to use this trait.

The second trait is insect resistance to particularly damaging worms due to the incorporation of a bacterial gene into the crop. The worms are killed by a protein before they can do damage.

The main benefit of these crops is to the growers in terms of better and easier control of worms or weeds. However the consumer benefits because the crops can be produced more economically. As a consequence, the produce will be less costly.

It is important to note that these crops first were grown on a large scale in the middle 1990s and, therefore, foods made have been in our food supply for nearly ten years now.

A number of new crops with potential to directly benefit the consumer will soon be introduced or are in research stages. An example of these is golden rice that has been genetically modified to provide pre-vitamin A. This new rice benefit those in cultures where rice forms the staple of their diet. In most of these cultures, vitamin A deficiency causes health problems.

Seed for insecticidal corn currently available to growers provides an example of the approval process for new genetically engineered crops. The proteins (cry1Ab and cry 1F) found in competitive varieties of this corn kill worms but have been judged safe to humans. The human health assessment was made by the EPA because of the proteins have insecticidal properties.

Both proteins have been found to be degraded by gastric fluids and inactivated by typical food processing. In acute toxicity in animal models both proteins were found to give no effects at levels comparable to those at which table salt would kill half the animals. The EPAs overall assessment was that the protein was safe for human consumption, including children.

Several related issues regarding segregation fall more squarely under agronomic concerns being handled by the Ag Commissioner. Still they could have an impact on human health should the food supply become contaminated, for instance, with a crop that had been transformed to produce a pharmaceutical.

The importance of segregation is emphasized by a couple of instances where GM crops not approved for the human consumption have got into the food supply. The most well know of these was the Starlink incident where a corn approved for animal feed was found in tacos.

Well up the list of potential health issues associated with GM crops is allergenic reactions caused by proteins. It is well established that proteins can cause allergenic reactions. But there are relatively few groups of plant allergens and these are well understood and methods are available to test for them.

Nonetheless, when a new food from conventional breeding the Kiwi was first marketed in the last century allergic reactions – some quite severe - were detected for the first time. Many other current foods are known to cause allergic reactions in some people. These are labeled appropriately under FDA rules. It is also important to note there that GM technology can potentially be used to remove allergens from foods, for instance soybeans.

The US regulatory system is based in an assessment of probable risks vs. the benefit of the technology. This is different from the systems used in some other parts of the world that are heavily influenced by the Precautionary Principle. Two definitions of the Precautionary Principle that can also be found below:

• *The concept of taking anticipatory action in the absence of complete proof of harm, particularly when there is scientific uncertainty about causal links (Jackson, 1993).*
• *The precautionary principle states that decision makers should act in advance of scientific certainty to prevent harm to humans and the environment (O'Riordan and Jordan, 1995).*

So the question will always be one of balance. There is a continuum of people in society from those that do not want any risk to those that climb mountains. This is important because as has pointed out earlier in this report, it is impossible to demonstrate absolute safety; and you can only test for what seems probable. Any system to assess the safety of a new technology will only cater to a portion of that society.

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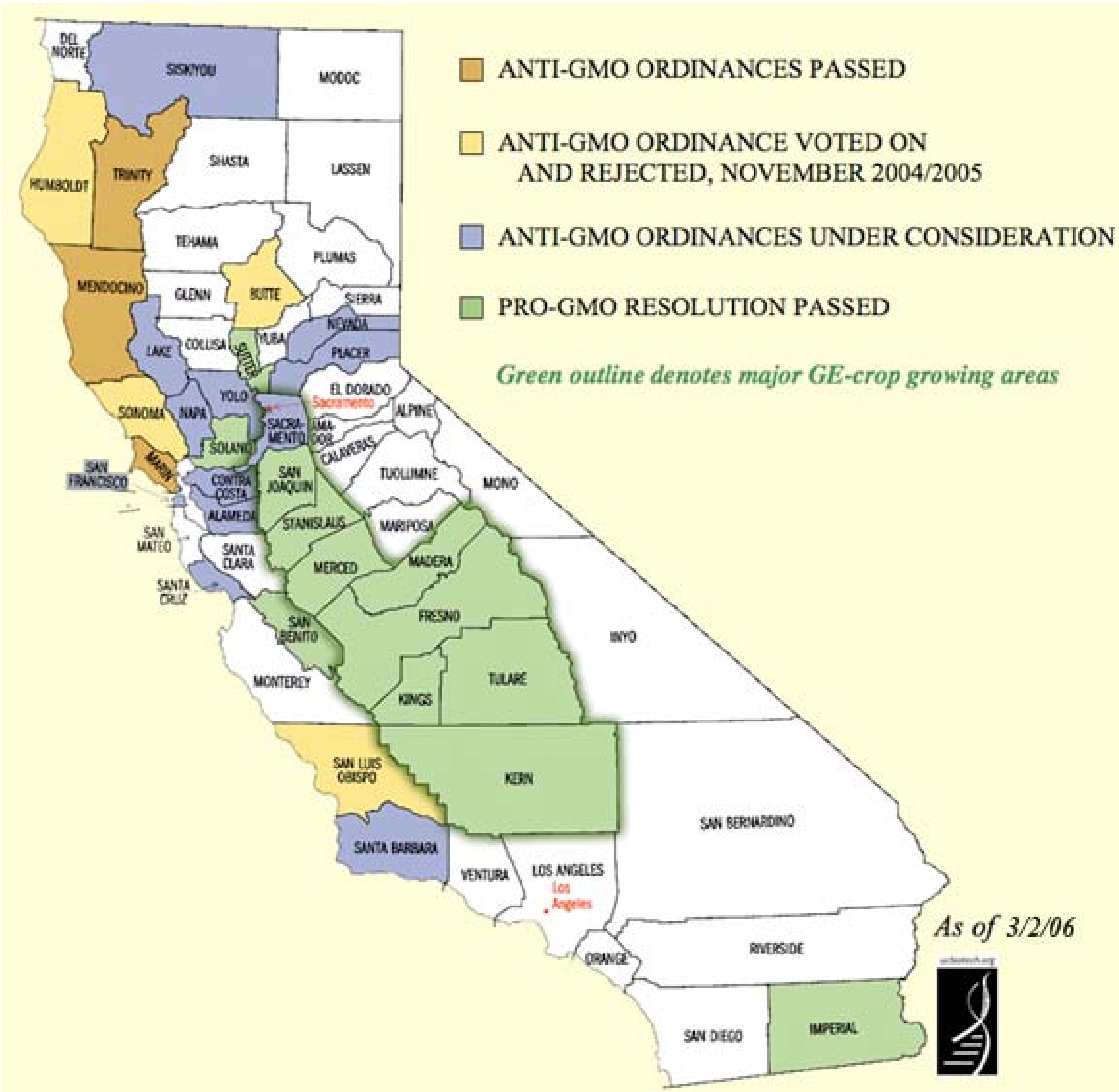
The US regulatory system is based in an assessment of probable risks vs. the benefit of the technology. This is different from the systems used in some other parts of the world that are heavily influenced by the Precautionary Principle. I have given two definitions of the Precautionary Principle . So the question will always be where is the balance. There is a continuum of people from those that do not want any risk to those that climb mountains. This is important because as Robbie has pointed out, it is impossible to demonstrate absolute safety. Any you can only test for what seems probable.

What Have Other Counties in California Done?

Map of California Counties - Status of Ordinances (as of 3/2/06)



In conclusion, since this all began with Measure Q (an anti-GMO ordinance), we felt it would be of interest to this audience to see how other counties in the state have approached this issue. The source of this map is the ucbiotec website at UC Berkley.

Anti-GMO Ordinances have passed in 3 counties: Trinity County passed an ordinance at the Board of Supervisors; Mendocino and Marin Counties by ballot issues.

Anti-GMO Issues have been defeated at the ballot box by 4 counties: San Luis Obispo, Sonoma, Butte and Humboldt.

Lake County had a proposed ordinance voted down by their Board of Supervisors.

13 counties have passed Pro-GMO Resolutions at their Boards of Supervisors.

The blue areas indicate Anti-GMO proposals under consideration – the only link for this category was a website called SB GE Free in Santa Barbara.

We hope that if, nothing else, the work of this task force demonstrates that regardless of political forces at work this is not an issue that can be simplified to just pro or con. It is, rather, a highly complex science that may affect our health in a variety of positive and/or negative aspects.

Glossary

GOVERNING AGENCIES:

APHIS - Animal and Plant Health Inspection Service
CODEX - Codex Alimentarius Commission
EPA - Environmental Protection Agency
FAO - Food and Agriculture Organization
FDA - Food and Drug Administration
NIH - National Institutes of Health
USDA - United States Department of Agriculture
WHO - World Health Organization

GLOSSARY OF TERMS:

Bt - Bacillius thuringensis, A species of soil borne bacteria from which a gene coding for one of the many endotoxins lethal to the high pH guts of caterpillar pests was engineered into several crop varieties for plant protection.

Genotype - a genetic make-up of an organism or group of organisms with reference to a single trait or group of traits, not visibly expressed. An assemblage of genes in an organism.

GMO - an organism that has a gene construct inserted via recombinant DNA technology.

GRAS - generally recognized as safe.

Hybridization - the formation of progeny by a mating between two organisms of different species.

Outcrossing - the production of offspring that originates when the sperm and egg come from genetically different plants.

Phenotype - the external visible apperance of an organism.

PIPs - Plant Incorporated Protectants.

rDNA - a molecule of DNA formed by the joining of segments from different sources.

Substantial Equivalence - the comparison of conventional or traditional breeding methods to biotech engineered or genetically engineered methods.

Trangenics - genetic engineering involving gene transfer within or among species or kingdoms

GMO Task Force - Reference Library (version 6/Final)

Topic: Peer Reviewed Journal Articles (Original Research: Health Implications)

Author(s)	Status	Date	Title	Source	Relevance to Task Force
Brake; Evenson	Filed	Jan-04	A generational study of glyphosate-tolerant soybeans on mouse fetal, postnatal, pubertal, and adult testicular development	Food & Chemical Toxicology. 42(1): 29-36	Feeding studies of Roundup Ready soy showing no deleterious effects
Ewen; Pusztai	Filed	Oct-99	Effect of diets containing genetically modified potatoes expressing *Galanthus nivalis* lectin on rat small intestine *****Includes lengthy written exchange between Pusztai and Ammann and others**	The Lancet. 354:1353-1354	Deleterious effects on mammalian gut observed in transgenic lectin feeding study
Hammond; et al	Filed	1996	The feeding value of soybeans fed to rats, chickens, catfish, and dairy cattle is not altered by genetic incorporation of glyphosate tolerance	Journal of Nutrition. 126: 717-727	GE feeding studies
Harrison; et al	Filed	1996	The expressed protein in glyphosate-tolerant soybean is rapidly digested in vitro and is not toxic to acutely gavaged mice.	Journal of Nutrition. 126: 728-740	GE feeding studies
Jackson; et al	Filed	Feb-01	Expression of mouse interleukin-4 by a recombinant ectromelia virus suppresses cytolytic lymphocyte responses and overcomes genetic resistance to mousepox.	Journal of Virology. 75:1205-1210	Unexpected effects of transgenic introduction
Jung; Sheaffer	Filed	Sep-04	Influence of Bt Transgenes on Cell Wall Lignification and Digestibility of Maize Stover for Silage	Crop Science. 44: 1781-1789	Lignin level issue
Matthews; et al	Filed	Sep-05	Toxic Secondary Metabolite Production in Genetically Modified Potatoes in Response to Stress	Journal of Agricultural and Food Chemistry. 53(20): 7766-7776	
Mentewab; Stewart	Filed	Sep-05	Overexpression of an *Arabidopsis thaliana* ABC transporter confers kanamycin resistance to transgenic plants	Nature Biotechnology. 23(9):1177-1180	An alternative method to using antibiotic resistant markers in transgenic plants
Netherwood; et al	Filed	Feb-04	Assessing the survival of transgenic plant DNA in the human gastrointestinal tract	Nature Biotechnology. 22(2):204-209	Possible transfer of transgenes from GM plants to intestinal microflora
Nordlee; et al	Filed	Mar-96	Identification of a Brazil-nut allergen in transgenic soybeans.	New England Journal of Medicine. 334:688-692	Allergenicity issue
Poerschmann; et al	Filed	Aug-05	Molecular Composition of Leaves and Stems of Genetically Modified Bt and Near-Isogenic Non-Bt Maize - Charaterization of Lignin Patterns	Journal of Environmental Quality. 34: 1508-1518	Lignin level issue
Prescott; et al	Filed	Oct-05	Transgenic Expression of Bean Amylase Inhibitor in Peas Results in Altered Structure and Immunogenicity	Journal of Agricultural and Food Chemistry. 53 (23): 9023-9030	Transgenic pea causes immune reactions not found in the original protein
Roessner; et al	Filed	Jan-01	Metabolic profiling allows comprehensive phenotyping of genetically or environmentally modified plant systems	The Plant Cell.13: 11-29	Presence of metabolites in transgenic plant cells not found in non-GE plants
Saxena; Stotzky	Filed	Sep-01	Bt Corn has a higher lignin content than non-Bt corn	American Journal of Botany. 88(9): 1704-1706	Potential nutritional/ecological implications in transgenic corn

Topic: Peer Reviewed Journals/Texts (Author Assessments and Research Summaries)

Author(s)	Status	Date	Title	Source	Relevance to Task Force
American Dietetic Association	Filed	Feb-06	Position of the American Dietetic Association: Agricultural and Food Biotechnology	Journal of the American Dietetic Association. 106(2): 285-293	Current assessment of the safety of ge foods by nutrition experts
Bennett; et al	Filed	Mar-04	An assessment of the risks associated with the use of antibiotic resistance genes in genetically modified plants: report of the Working Party of the British Society for Antimicrobial Chemotherapy	Journal of Antimicrobial Chemotherapy. 53(3): 418-431	Antibiotic resistant marker genes topic
Bradford; et al	Filed	Apr-05	Regulating transgenic crops sensibly: lessons from plant breeding, biotechnology and genomics *****Includes lengthy written exchange between Bradford and Schubert**	Nature Biotechnology. 23(4): 439-444	Evaluation of transgenic regulations
Buchanan, B.	Filed	May-01	Genetic engineering and the allergy issue.	Plant Physiology. 126: 5-7	Allergy Issues

Freese; Schubert	Filed	Nov-04	Safety Testing and Regulation of Genetically Engineered Foods	Biotechnology and Genetic Engineering Reviews. 21: 299-324	Thorough summary of potential problems of GE foods
Mayeno; Gleich	Filed	Sep-94	Eosiniphilia-Myalgia syndrome and tryptophan production: A cautionary tale.	Trends in Biotechnology. 12: 346-352	Tryptophan poisoning issue
National Academy of Sciences	Full Report Available	Jul-04	Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects	National Academy of Sciences	Comprehensive overview of assessing the unintended health effects of GE
Pusztai; Bardocz	Filed	Oct-05	GMO in Animal Nutrition: potential benefits and risks	Biology of Nutrition in Growing Animals; Chapter 17	Thorough review of published GMO animal feeding studies
Roufs, B.	Filed	Jul-92	Review of L-tryptophan and eosiniphilia-myalgia syndrome.	Journal of the American Dietetic Association. 92(7): 844-850	Tryptophan Poisoning Issue
World Health Organization	Filed	2005	Modern food biotechnology, human health and development: an evidence based study	World Health Organization	Comprehensive assessment of risks and benefits of GE foods
Topic: Peer Reviewed Journal Articles (Original Research: Environmental Concerns and Other Issues)					
Author(s)	**Status**	**Date**	**Title**	**Source**	**Relevance to Task Force**
Chapela; Quist	Filed	Nov-01	Transgenic DNA introgressed into traditional maize landraces in Oaxaca, Mexico	Nature. 414: 541-543	Report of transgenic sequences present in traditional varieties of maize
Holmes; et al	Filed	Jan-99	Effects of *Klebsiella planticola* SDF20 on soil biota and wheat growth in sandy soil	Applied Soil Ecology. 11(1):67-78	Effects of GE crops on soil biota
Huang; et al	Filed	Apr-05	Insect-resistant GM rice in farmers' fields: Assessing productivity and health effects in China	Science. 308: 688-690	Study showing reduced pesticide use and exposure when using GE crops
Ortiz-Garcia; et al	Filed	Aug-05	Absence of detectable transgenes in local landraces of maize in Oaxaca, Mexico (2003-2004)	Proceedings of the NAS. 102(35): 12338-12343	Original research that raises questions about Quist and Chapela's articles
Qaim; Zilberman	Filed	Feb-03	Yield effects of genetically modified crops in developing countries.	Science. 299: 900-902	Study showing reduced pesticide use and exposure when using GE crops
Watrud; et al	Filed	Oct-04	Evidence for landscape-level, pollen-mediated gene flow from genetically modified creeping bentgrass with CP4 EPSPS as a marker	Proceedings of the NAS. 101(40): 14533-14538	Evidence of gene flow from a GE grass up to 21 km away from test plot
Ye; et al	Filed	Jan-00	Engineering the Provitamin A Biosynthetic Pathway into (Carotenoid-Free) Rice Endosperm	Science. 287: 303-305	A look at the potential of using transgenics to deliver vital nutrients
Topic: GMO Regulatory Information (includes Regulatory Analysis and Critique)					
Author(s)	**Status**	**Date**	**Title**	**Source**	**Relevance to Task Force**
Andow; et al	Filed	Dec-04	A Growing Concern: Protecting the Food Supply in an Era of Pharmaceutical and Industrial Crops	Union of Concerned Scientists Published Report	Detailed critique of the use of food crops for "pharma" crops
Caplan	Free Online	Jun-03	Raising Risk: Field Testing of Genetically Engineered Crops in the United States http://www.uspirg.org/reports/RaisingRisk2003.pdf	U.S. PIRG Education Fund	Critical view of field testing GE crops; extensive reference list
Chassy; et al	Filed	Oct-01	Evaluation of the U.S. Regulatory Process for Crops Developed through Biotechnology	CAST Issue Paper (Council for Agricultural Science and Technology)	Good overview of how the GMO regulatory process operates
Commission of the European Communities	Filed	Feb-00	Communication From The Commission on the Precautionary Principle	Comission of the European Communities	Summary of the precautionary principle
Gurian-Sherman	Free Online	Jan-03	Holes in the Biotech Safety Net: FDA Policy Does Not Assure the Safety of Genetically Engineered Foods http://www.cspinet.org/new/pdf/fda_report__final.pdf	Center For Science In The Public Interest	A critical look at FDA's oversight of GE crops, especially as it pertains to future GE crops

Mellon; Rissler	Filed	2004	Gone To Seed: Transgenic Contaminants in the Traditional Seed Supply	Union of Concerned Scientists Published Report	Report indicating transgenic presence in the non-GMO seed supply
National Academy of Sciences	Filed	Jun-05	Safety of Genetically Engineered Foods. Approaches to Assessing Unintended Health Effects. Preface and Executive Summary	National Academies Press	Report document commissioned by the FDA, EPA, and USDA. to compile recommendations for procedures to ensure new GM foods have had a thorough assessment.
Stewart; Wheaton	Filed	2003	Urban Myths and Scientific Facts about the Biosafety of Genetically Modified (GM) Crops, Chapter 20, Chrispeels and Sadava Textbook	Plants, Genes, and Crop Biotechnology (2nd Ed.)	Critical look at some of the concerns often cited over GM Crops
USDA, Office of Inspector General	Free Online	Dec-05	Audit Report: Animal and Plant Health Inspection Service Controls Over Issuance of Genetically Engineered Organism Release Permits http://www.usda.gov/oig/webdocs/50601-08-TE.pdf	Office of Inspector General - Southwest Region	Critique of USDA APHIS ' oversight of proposed GE crop's field testing
US EPA	Filed	Oct-06	Pp 13-19, 110-111.	Biopesticides and Pollution	GM crops as relates to products with
Topic: Magazine Articles/Web Articles (Not Peer Reviewed)					
Author(s)	**Status**	**Date**	**Title**	**Source**	**Relevance to Task Force**
Ferber	Filed	Mar-03	Something Funny Down on the Pharm	Popular Science	Pharm crops getting into food supply
Gibbs	Filed	Nov-03	The Unseen Genome: Gems among the Junk	Scientific American	Explains junk (non-protein coding) DNA; implications for genetic engineering?
Manning	Filed	May-04	Super Organics	Wired	Explanation of researchers using biotech to improve crops w/o gene insertion
Wheelwright	Filed	Mar-01	How a genetically modified corn called StarLink that wasn't intended for human got into your food supply	Discover	StarLink case-study; indicates common co-mingling of crops in the food supply